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☐ 1: Eur J Nucl Med. 1998 Oct;25(10):1383-9.

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## Imaging of metastatic melanoma utilising a technetium-99m labelled RGD-containing synthetic peptide.

Sivolapenko GB, Skarlos D, Pectasides D, Stathopoulou E, Milonakis A, Sirmalis G, Stuttle A, Courtenay-Luck NS, Konstantinides K, Epenetos AA.

Encephalos Research and Therapeutic Institute, Athens, Greece.

Integrins are cell-surface glycoproteins found in different forms on all cells except erythrocytes. Integrins bind to cell adhesion molecules and to proteins found in the extracellular matrix. A tripeptidic sequence Arg-Gly-Asp (RGD) is often the primary site of recognition by integrins which are expressed on tumour cells and are responsible for tumour invasion and metastasis. A synthetic decapeptide designated alpha P2 containing two RGD sequences radiolabelled with technetium-99m was used to image malignant melanoma in vivo. Fourteen patients previously diagnosed with metastatic melanoma underwent gamma camera imaging 20-180 min following intravenous administration of the radiolabelled synthetic decapeptide alpha P2. Six out of eight (6/8) of the lymph node metastases (75%) and all other neoplastic sites (11 sites) were successfully imaged, with the exception of three sites in the mediastinal area which were not positively imaged. In two cases there was false positive uptake in the rounded pigmented-areolar/nipple area. In three cases (seven sites) the peptide scan confirmed the absence of disease in suspected lesions (true-negative). The synthetic peptide was rapidly removed from the circulation by filtration through the kidneys and excretion in the urine. No toxicity or adverse events were recorded. Radiolabelled alpha P2 peptide, which binds specifically to adhesion molecules on tumours, can be used for the in vivo detection of neoplastic metastases.

Publication Types:

- Clinical Trial

PMID: 9818277 [PubMed - indexed for MEDLINE]

## 8. Document ID: US 6180084 B1

L11: Entry 8 of 8

File: USPT

Jan 30, 2001

DOCUMENT-IDENTIFIER: US 6180084 B1

**\*\* See image for Certificate of Correction \*\***

TITLE: NGR receptor and methods of identifying tumor homing molecules that home to angiogenic vasculature using same

Detailed Description Text (65):

Where a tumor homing molecule is a nucleic acid or is tagged with a nucleic acid, an assay such as PCR can be particularly useful for identifying the presence of the molecule because, in principle, PCR can detect the presence of a single nucleic acid molecule (see, for example, Erlich, PCR Technology: Principles and Applications for DNA Amplification (Stockton Press 1989), which is incorporated herein by reference). Preliminary studies have demonstrated that, following intravenous injection of 10 ng of an approximately 6000 base pair plasmid into a mouse and 2 minutes in the circulation, the plasmid was detectable by PCR in a sample of lung. These results indicate that nucleic acids are sufficiently stable when administered into the circulation such that in vivo panning can be used to identify nucleic acid molecules that selectively home to a tumor.

Detailed Description Text (151):

Tumor homing molecules obtained using the methods disclosed herein also can be useful for identifying a target molecule such as a cell surface receptor or a ligand for a receptor, which is recognized by the tumor homing peptide, or for substantially isolating the target molecule. For example, a tumor homing peptide can be linked to a solid support such as a chromatography matrix. The linked peptide then can be used for affinity chromatography by passing an appropriately processed sample of a tumor over the column in order to bind a particular target molecule. The target molecule, which forms a complex with the tumor homing molecule, then can be eluted from the column and collected in a substantially isolated form. The substantially isolated target molecule then can be characterized using well known methods. A tumor homing peptide also can be linked to a detectable moiety such as a radionuclide, a fluorescent molecule, an enzyme or biotin and can be used, for example, to screen a sample in order to detect the presence of the target molecule in a tumor or to follow the target molecule during various isolation steps.

Detailed Description Text (165):

The disclosed in vivo panning method can be used to detect four different kinds of target molecules in tumors. First, because tumor vasculature undergoes active angiogenesis, target molecules that are characteristic of angiogenic vasculature, in general, or angiogenic tumor vasculature, in particular, can be identified. Second, vascular target molecules that are characteristic of the tissue of origin of the tumor can be identified. Third, target molecules that are expressed in the vasculature of a particular type of tumor can be identified. Fourth, tumor stroma or tumor cell target molecules can be identified due to the fenestrated nature of tumor vasculature, which allows the potential tumor homing molecules to leave the circulation and contact the tumor parenchyma.

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